**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1-16. (canceled)

17. (currently amended) A method for imaging a pulmonary embolus comprising the steps of:

a. localizing a radiolabelled compound at the pulmonary embolus;

b. acquiring image slices representing a physical property of the concentration of radioactivity within the radiolabelled pulmonary embolus;

c. assembling the image slices into a three-dimensional matrix of data;

d. scanning the three-dimensional matrix of data along an array of parallel lines to determine a maximum value along each line; and

e. assigning the maximum value along each line to a pixel in a two-dimensional array, the position of the pixel corresponding to the position of the line in the array of parallel lines.

18. (canceled)

19. (canceled)

20.(previously added) The method of Claim 17 wherein the localization step comprises the step of localizing a compound of the formula (I), and pharmaceutically acceptable salts thereof, at the thrombus:

$$|(Q)d'-L_n-C_{h'}|_{X-M_T(A_{L1})y(A_{L2})z}$$

(I),

wherein,

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT
REPLY FILED UNDER EXPEDITED
PROCEDURE PURSUANT TO
37 CFR § 1.116

Q is a glycoprotein IIb/IIIa binding compound;

d' is 1 - 20;

Ln is a linking group of formula:

$$M^{1}-[Y^{1}(CR^{55}R^{56})f(Z^{1})f'Y^{2}]f-M^{2},$$

wherein:

$$M^1$$
 is -[(CH2)gZ<sup>1</sup>]g'-(CR<sup>55</sup>R<sup>56</sup>)g''-;

$${
m M}^2$$
 is -(CR<sup>55</sup>R<sup>56</sup>)g"-[Z<sup>1</sup>(CH<sub>2</sub>)g]g'-;

g is independently 0-10;

g' is independently 0-1;

g" is independently 0-10;

f is independently 0-10;

f is independently 0-10;

f" is independently 0-1;

 $Y^1$  and  $Y^2$ , are independently selected at each occurrence from: a bond, O, NR<sup>56</sup>, C=O, C(=O)O, OC(=O)O, C(=O)NH-, C=NR<sup>56</sup>, S, SO, SO<sub>2</sub>, SO<sub>3</sub>, NHC(=O), (NH)<sub>2</sub>C(=O), and (NH)<sub>2</sub>C=S;

**Application No.:** 09/534,893

Office Acti n Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 $Z^1$  is independently selected at each occurrence from a C6-C14 saturated, partially saturated, or aromatic carbocyclic ring system, substituted with 0-4  $R^{57}$ ; and a heterocyclic ring system, substituted with 0-4  $R^{57}$ ;

R<sup>55</sup> and R<sup>56</sup> are independently selected at each occurrence from: hydrogen; C1-C10 alkyl substituted with 0-5 R<sup>57</sup>; and alkaryl wherein the aryl is substituted with 0-5 R<sup>57</sup>;

 $R^{57}$  is independently selected at each occurrence from the group: hydrogen, OH, NHR<sup>58</sup>, C(=O)R<sup>58</sup>, OC(=O)R<sup>58</sup>, OC(=O)OR<sup>58</sup>, C(=O)OR<sup>58</sup>, C(=O)NR<sup>58</sup>, C=N, SR<sup>58</sup>, SOR<sup>58</sup>, SO2R<sup>58</sup>, NHC(=O)R<sup>58</sup>, NHC(=O)NHR<sup>58</sup>, NHC(=S)NHR<sup>58</sup>; or, alternatively, when attached to an additional molecule Q, R<sup>57</sup> is independently selected at each occurrence from the group: O, NR<sup>58</sup>, C=O, C(=O)O, OC(=O)O, C(=O)N-, C=NR<sup>58</sup>, S, SO, SO2, SO3, NHC(=O), (NH)2C(=O), (NH)2C(=S); and,

R<sup>58</sup> is independently selected at each occurrence from the group: hydrogen; C1-C6 alkyl; benzyl, and phenyl;

M<sub>T</sub> is a transition metal radionuclide;

 $C_{h'}$  is a radionuclide metal chelator or bonding unit bound to the transition metal radionuclide selected from the group consisting of:  $R^{40}N=N^{+}=$ ,  $R^{40}R^{41}N-N=$ ,  $R^{40}N=N(H)-$ ;

 $R^{40}$  is independently selected at each occurrence from the group: a bond to Ln, C1-C 10 alkyl substituted with 0-3  $R^{52}$ , aryl substituted with 0-3  $R^{52}$ , cycloaklyl substituted with 0-3  $R^{52}$ , heterocycle substituted with 0-3  $R^{52}$ , heterocycloalkyl substituted with 0-3  $R^{52}$ , aralkyl substituted with 0-3  $R^{52}$ ;

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 $R^{41}$  is independently selected from the group: hydrogen, aryl substituted with 0-3  $R^{52}$ ,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{52}$ , and a heterocycle substituted with 0-3  $R^{52}$ ;

 $R^{52} \text{ is independently selected at each occurrence from the group: a bond to $L_n$, =0,} \\ F, Cl, Br, I,-CF3,-CN, -CO2R^{53}, -C(=O)R^{53}, -C(=O)N(R^{53})2, -CHO, -CH2OR^{53}, \\ -OC(=O)R^{53}, -OC(=O)OR^{53a}, -OR^{53}, -OC(=O)N(R^{53})2, -NR^{53}C(=O)R^{53}, -NR^{54}C(=O)R^{53}, -NR^{54}C(=O)R^$ 

 $R^{53}$ ,  $R^{53a}$ , and  $R^{54}$  are each independently selected at each occurrence from the group: hydrogen, C1-C6 alkyl, and a bond to  $L_n$ ;

A<sub>L1</sub> is a first ligand wherein each of the y first ligands are selected from the group consisting of: dioxygen ligands, functionalized aminocarboxylates, halides, and combinations thereof;

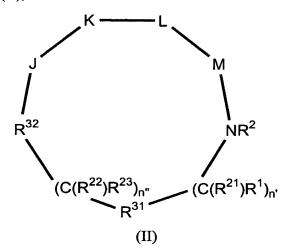
 $A_{L2}$  is a second ligand wherein each of the z second ligands are selected from the group consisting of: trisubstituted phosphines, trisubstituted arsines, tetrasubstituted diphosphines, tetrasubstituted diarsines, and combinations thereof;

x is independently 1-2;

y is independently 1-2; and

z is independently 0-4.

- 21. (previously added) The method of Claim 20 wherein M<sub>T</sub> is selected from the group consisting of: technetium-99m, rhenium-186, and rhenium-188.
- 22. (previously added) The method of Claim 20 wherein the localization step comprises the step of localizing a compound of the formula (I) at the pulmonary embolus wherein Q is of the formula (II),



or a pharmaceutically acceptable salt or prodrug form thereof wherein:

 $R^{31}$  is a C6-C14 saturated, partially saturated, or aromatic carbocyclic ring system substituted with 0-4  $R^{10}$  or  $R^{10a}$ ;

R<sup>32</sup> is selected from:

- -C(=O)-;
- -C(=S)-
- -S(=O)2-;
- -S(=O)-;
- $-P(=Z)(ZR^{13})-;$

Z is S or O;

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

n" and n' are independently 0-2;

 $R^1$  and  $R^{22}$  are independently selected from the following groups:

hydrogen,

C1-C8 alkyl substituted with 0-2 R<sup>11</sup>;

C2-C8 alkenyl substituted with 0-2 R<sup>11</sup>;

C2-C8 alkynyl substituted with 0-2 R<sup>11</sup>;

C3-C10 cycloalkyl substituted with 0-2 R<sup>11</sup>;

aryl substituted with 0-2 R<sup>12</sup>;

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R<sup>12</sup>;

=O, F, Cl, Br, I, -CF3, -CN, -CO2R<sup>13</sup>, -C(=O)R<sup>13</sup>, -C(=O)N(R<sup>13</sup>)2, -CHO, -CH2OR <sup>13</sup>, -OC(=O)R<sup>13</sup>, -OC(=O)OR<sup>13a</sup>, -OC(=O)OR<sup>13a</sup>, -OC(=O)N(R<sup>13</sup>)2, -NR<sup>13</sup>C(=O)R<sup>13</sup>, -NR<sup>14</sup> C(=O)OR<sup>13a</sup>, -NR<sup>13</sup>C(=O)N(R<sup>13</sup>)2, -NR<sup>14</sup>SO2N(R<sup>13</sup>)2, -NR<sup>14</sup>SO2R<sup>13a</sup>, -SO3H, -SO2R <sup>13a</sup>, -SR<sup>13</sup>, -S(=O)R<sup>13a</sup>, -SO2N(R<sup>13</sup>)2, -N(R<sup>13</sup>)2, -NHC(=NH)NHR<sup>13</sup>, -C(=NH)NHR<sup>13</sup>, -NOR<sup>13</sup>, NO2, -C(=O)NHOR<sup>13</sup>, -C(=O)NHNR<sup>13</sup>R<sup>13a</sup>, -OCH2CO2H, <sup>2</sup>-(1-morpholino)ethoxy;

 $R^1$  and  $R^{21}$  can alternatively join to form a 3-7 membered carbocyclic ring substituted with 0-2  $R^{12}$ ;

when n' is 2,  $R^1$  or  $R^{21}$  can alternatively be taken together with  $R^1$  or  $R^{21}$  on an adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between said carbon atoms;

Application No.: 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 $R^{22}$  and  $R^{23}$  can alternatively join to form a 3-7 membered carbocyclic ring substituted with 0-2  $R^{12}$ ;

when n" is 2,  $R^{22}$  or  $R^{23}$  can alternatively be taken together with  $R^{22}$  or  $R^{23}$  on an adjacent carbon atom to form a direct bond, thereby to form a double or triple bond between the adjacent carbon atoms;

 $R^1$  and  $R^2$ , where  $R^{21}$  is H, can alternatively join to form a 5-8 membered carbocyclic ring substituted with 0-2  $R^{12}$ ;

R<sup>11</sup> is selected from one or more of the following:

=O, F, Cl, Br, I, -CF3, -CN, -CO2R<sup>13</sup>, -C(=O)R<sup>13</sup>, -C(=O)N(R<sup>13</sup>)2, -CHO, -CH2OR <sup>13</sup>, -OC(=O)R<sup>13</sup>, -OC(=O)OR<sup>13a</sup>, -OR<sup>13</sup>, -OC(=O)N(R<sup>13</sup>)2, -NR<sup>13</sup>C(=O)R<sup>13</sup>, -NR<sup>14</sup> C(=O)OR<sup>13a</sup>, -NR<sup>13</sup>C(=O)N(R<sup>13</sup>)2, -NR<sup>14</sup>SO2N(R<sup>13</sup>)2, -NR<sup>14</sup>SO2R<sup>13a</sup>, -SO3H, -SO2R <sup>13a</sup>, -SR<sup>13</sup>, -S(=O)R<sup>13a</sup>, -SO2N(R<sup>13</sup>)2, -N(R<sup>13</sup>)2, -NHC(=NH)NHR<sup>13</sup>, -C(=NH)NHR<sup>13</sup>, -NOR<sup>13</sup>, NO2, -C(=O)NHOR<sup>13</sup>, -C(=O)NHNR<sup>13</sup>R<sup>13a</sup>, -OCH2CO2H, <sup>2-(1-morpholino)ethoxy</sup>,

C1-C5 alkyl, C2-C4 alkenyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C2-C6 alkoxyalkyl, C3-C6 cycloalkoxy, C1-C4 alkyl (alkyl being substituted with 1-5 groups selected independently from: -NR<sup>13</sup>R<sup>14</sup>, -CF3, NO2, -SO2R<sup>13a</sup>, or -S(=O)R<sup>13a</sup>),

aryl substituted with 0-2 R<sup>12</sup>,

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, said heterocyclic ring being substituted with 0-2 R<sup>12</sup>;

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R<sup>12</sup> is selected from one or more of the following:

phenyl, benzyl, phenethyl, phenoxy, benzyloxy, halogen, hydroxy, nitro, cyano, C1-C 5 alkyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C7-C10 arylalkyl, C1 -C5 alkoxy, -C02 $R^{13}$ , -C(=0)NHOR<sup>13a</sup>, -C(=0)NHN( $R^{13}$ )2, =NOR<sup>13</sup>, -B( $R^{34}$ )( $R^{35}$ ), C3 -C6 cycloalkoxy,  $-OC(=O)R^{13}$ ,  $-C(=O)R^{13}$ ,  $-OC(=O)OR^{13}$ ,  $-OR^{13}$ ,  $-(C_1-C_4)OR^{13}$  $^{13}$ ,  $^{-N(R^{13})2}$ ,  $^{-OC(=O)N(R^{13})2}$ ,  $^{-NR^{13}C(=O)R^{13}}$ ,  $^{-NR^{13}C(=O)OR^{13a}}$ ,  $^{-NR^{13}}$  $C(=O)N(R^{13})2$ ,  $-NR^{13}SO2N(R^{13})2$ ,  $-NR^{13}SO2R^{13a}$ , -SO3H,  $-SO2R^{13a}$ ,  $-S(=O)R^{13a}$ , -SR<sup>13</sup>, -SO<sub>2</sub>N(R<sup>13</sup>)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl, methylenedioxy, ethylenedioxy, C<sub>1</sub>-C<sub>4</sub> haloalkyl. C1-C4 haloalkoxy, C1-C4 alkylcarbonyloxy, C1-C4 alkylcarbonyl, C1-C4 alkylcarbonylamino, -OCH2CO2H, 2-(1-morpholino)ethoxy, C1-C4 alkyl (alkyl being substituted with  $-N(R^{13})_2$ , -CF3, NO2, or -S(=0) $R^{13a}$ );

R<sup>13</sup> is selected independently from: H, C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1-C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

R<sup>13a</sup> is C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1 -C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

when two R<sup>13</sup> groups are bonded to a single N, said R<sup>13</sup> groups may alternatively be taken together to form -(CH2)2-5- or -(CH2)O(CH2)-;

R<sup>14</sup> is OH, H, C<sub>1</sub>-C<sub>4</sub> alkyl, or benzyl:

R<sup>21</sup> and R<sup>23</sup> are independently selected from:

hydrogen:

C1-C4 alkyl, optionally substituted with 1-6 halogen;

**DOCKET NO.:** DM6993/BMS-0689 **Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

benzyl;

R<sup>2</sup> is H or C1-C8 alkyl;

R<sup>10</sup> and R<sup>10a</sup> are selected independently from one or more of the following: phenyl, benzyl, phenethyl, phenoxy, benzyloxy, halogen, hydroxy, nitro, cyano, C1-C C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C7-C10 arylalkyl, C1 5 alkyl, -C5 alkoxy,  $-CO2R^{13}$ ,  $-C(=O)N(R^{13})2$ ,  $-C(=O)NHOR^{13}a$ ,  $-C(=O)NHN(R^{13})2$ ,  $=NOR^{13}$ ,  $-B(R^{34})(R^{35})$ , C3-C6 cycloalkoxy,  $-OC(=O)R^{13}$ ,  $-C(=O)R^{13}$ ,  $-OC(=O)OR^{13a}$ ,  $-OR^{13}$ ,  $-(C^{34})(R^{35})$ 1-C4 alkyl)- $OR^{13}$ ,  $-N(R^{13})$ 2,  $-OC(=O)N(R^{13})$ 2,  $-NR^{13}C(=O)R^{13}$ ,  $-NR^{13}C(=O)OR^{13}$ a,  $-NR^{13}C(=O)N(R^{13})2$ ,  $-NR^{13}SO_2N(R^{13})2$ ,  $-NR^{13}SO_2R^{13}a$ ,  $-SO_3H$ ,  $-SO_2R^{13}a$ , -S(=O)R<sup>13a</sup>, -SR<sup>13</sup>, -SO<sub>2</sub>N(R<sup>13</sup>)<sub>2</sub>, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl, methylenedioxy, ethylenedioxy, C<sub>1</sub> -C4 haloalkyl (including -CvFw where v = 1 to 3 and w = 1 to (2v+1)), C1-C4 haloalkoxy, C1-C4 alkylcarbonyloxy, C1-C4 alkylcarbonyl, C1-C4 -OCH2CO2H, 2-(1-morpholino)ethoxy, C1-C4 alkyl (alkyl being alkylcarbonylamino, substituted with  $-N(R^{13})_2$ ,  $-CF_3$ ,  $NO_2$ , or  $-S(=O)R^{13}a$ );

J is 3-aminopropionic acid or an L-isomer or D-isomer amino acid of structure  $-N(R^3)C(R^4)(R^5)C(=0)$ -, wherein:

R<sup>3</sup> is H or C1-C8 alkyl;

R<sup>4</sup> is H or C1-C3 alkyl;

R<sup>5</sup> is selected from:

hydrogen;

C1-C8 alkyl substituted with 0-2 R<sup>11</sup>;

C2-C8 alkenyl substituted with 0-2 R<sup>11</sup>;

Page 10 of 23

Application No.: 09/534,893 Office Action Dated: April 11, 2003 PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

C2-C8 alkynyl substituted with 0-2 R<sup>11</sup>;
C3-C10 cycloalkyl substituted with 0-2 R<sup>11</sup>:

aryl substituted with 0-2 R<sup>12</sup>;

a 5-10-membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, or O, said heterocyclic ring being substituted with 0-2 R<sup>12</sup>;

 $= O, F, Cl, Br, I, -CF3, -CN, -CO2R^{13}, -C(=O)R^{13}, -C(=O)N(R^{13})2, -CH0, -CH2OR^{13}, -OC(=O)R^{13}, -OC(=O)OR^{13}a, -OR^{13}, -OC(=O)N(R^{13})2, -NR^{13}C(=O)R^{13}, -NR^{14} \\ C(=O)OR^{13}a, -NR^{13}C(=O)N(R^{13})2, -NR^{14}SO2N(R^{13})2, -NR^{14}SO2R^{13}a, -SO3H, -SO2R^{13}a, -SR^{13}, -S(=O)R^{13}a, -SO2N(R^{13})2, -N(R^{13})2, -NHC(=NH)NHR^{13}, -C(=NH)NHR^{13}, -C(=NH)NHR^{13}, -C(=O)NHOR^{13}, -C(=O)NHOR^{13}, -C(=O)NHNR^{13}R^{13}a, -NOR^{13}, -B(R^{34})(R^{35}), -OCH2^{13}CO2H, 2-(1-morpholino)ethoxy, -SC(=NH)NHR^{13}, N3, -Si(CH3)3, (C1-C5 alkyl)NHR^{16}; -(C0-C6 alkyl)X;$ 

$$--$$
 (CH<sub>2</sub>)q  $--$  X

, where q is independently 0,1;

$$---$$
CH $_2$ 

 $-(CH_2)mS(O)p'(CH_2)2X$ , where m = 1,2 and p' = 0-2;

and

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 $R^3$  and  $R^4$  may also be taken together to form

$$(CH_2)_nX$$
 $-CH_2CHCH_2$ , where  $n = 0,1$  and  $X$  is

 $R^3$  and  $R^5$  can alternatively be taken together to form -(CH2)t- or -CH2S(O)p'C(CH3)2-, where t=2-4 and p'=0-2; or

 $R^4$  and  $R^5$  can alternatively be taken together to form -(CH2)u-, where u = 2-5;

R<sup>16</sup> is selected from:

an amine protecting group;

1-2 amino acids;

1-2 amino acids substituted with an amine protecting group;

K is a D-isomer or L-isomer amino acid of structure  $-(R^6)CH(R^7)C(=O)$ -, wherein:

R<sup>6</sup> is H or C1-C8 alkyl;

R<sup>7</sup> is selected from:

-(C1-C7 alkyl)X;

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

, wherein each q is independently 0-2 and

substitution on the phenyl is at the 3 or 4 position;

, wherein each q is independently 0-2

and substitution on the cyclohexyl is at the 3 or 4 position;

$$-(C_1-C_6 \text{ alkyl})$$

$$NH$$

$$0-3$$

-(CH2)mO-(C1-C4 alkyl)-X, where m = 1 or 2;

-(CH2)mS(O)p'-(C1-C4 alkyl)-X, where m = 1 or 2 and p' = 0-2; and

X is selected from:

 $-N(R^{13})R^{13}$ ;  $-C(=NH)(NH_2)$ ;  $-SC(=NH)-NH_2$ ; -NH-C(=NH)(NHCN);  $-NH-C(=NCN)(NH_2)$ ;  $-NH-C(=N-OR^{13})(NH_2)$ ;

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R<sup>6</sup> and R<sup>7</sup> can alternatively be taken together to form

$$(CH_2)_qX$$
 $(CH_2)_qCH(CH_2)_q$  , wherein each q is independently 1 or 2 and wherein

n = 0 or 1 and X is -NH2 or

L is -Y(CH2)vC(=O)-, wherein:

Y is NH, N(C1-C3 alkyl), O, or S; and v = 1 or 2;

M is a D-isomer or L-isomer amino acid of structure

$$\begin{array}{c|c}
R^{17} & H & C \\
\hline
 & C \\
 & (CH(R^4))_{q'} \\
 & R^8 \\
\end{array}$$
, wherein

q' is 0-2;

R<sup>17</sup> is H, C1-C3 alkyl;

R<sup>8</sup> is selected from:

-CO2R<sup>13</sup>,-SO3R<sup>13</sup>, -SO2NHR<sup>14</sup>, -B(R<sup>34</sup>)(R<sup>35</sup>), -NHSO2CF3, -CONHNHSO2CF3, -PO(OR<sup>13</sup>)2, -PO(OR<sup>13</sup>)R<sup>13</sup>, -SO2NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O), -SO2 NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O), -SO2NHCOR<sup>13</sup>, -CONHSO2R<sup>13a</sup>, -CH2CONHSO2R 13a, -NHSO2NHCOR<sup>13a</sup>, -NHCONHSO2R<sup>13a</sup>, -SO2NHCONHR<sup>13</sup>;

Page 14 of 23

**Application No.:** 09/534,893

Office Acti n Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R<sup>34</sup> and R<sup>35</sup> are independently selected from:

-OH,

-F,

 $-N(R^{13})2$ , or

C1-C8-alkoxy;

 $R^{34}$  and  $R^{35}$  can alternatively be taken together form:

a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a divalent cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O;

a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1-4 heteroatoms independently selected from N, S, or O.

23. (previously added) The method of Claim 22 wherein the localization step comprises the step of localizing a compound of the formula (I) at the pulmonary embolus wherein Q is of the formula (III),

Page 15 of 23

Office Acti n Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

or a pharmaceutically acceptable salt or prodrug form thereof wherein:

the shown phenyl ring may be further substituted with 0-3 R<sup>10</sup>;

R<sup>10</sup> is selected independently from: H, C1-C8 alkyl, phenyl, halogen, or C1-C4 alkoxy;

- R<sup>1</sup> is H, C1-C4 alkyl, phenyl, benzyl, or phenyl-(C1-C4)alkyl;
- R<sup>2</sup> is H or methyl;

R<sup>13</sup> is selected independently from: H, C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1-C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

R<sup>13a</sup> is C1-C10 alkyl, C3-C10 cycloalkyl, C4-C12 alkylcycloalkyl, aryl, -(C1-C10 alkyl)aryl, or C3-C10 alkoxyalkyl;

when two  $R^{13}$  groups are bonded to a single N, said  $R^{13}$  groups may alternatively be taken together to form -(CH2)2-5- or -(CH2)O(CH2)-;

 $R^{14}$  is OH, H, C1-C4 alkyl, or benzyl;

J is  $\beta$ -alanine or an L-isomer or D-isomer amino acid of structure -N(R<sup>3</sup>)C(R<sup>4</sup>)(R<sup>5</sup>)C(=O)-, wherein:

R<sup>3</sup> is H or CH3;

R<sup>4</sup> is H or C1-C3 alkyl;

R<sup>5</sup> is H, C1-C8 alkyl, C3-C6 cycloalkyl, C3-C6 cycloalkylmethyl, C1-C6 cycloalkylethyl, phenyl, phenylmethyl, CH2OH, CH2SH, CH2OCH3, CH2SCH3, CH2CH2 SCH3, (CH2)sNH2, -(CH2)sNHC(=NH)(NH2), -(CH2)sNHR<sup>16</sup>, where s = 3-5; or

R<sup>16</sup> is selected from:

an amine protecting group;

1-2 amino acids; or

1-2 amino acids substituted with an amine protecting group;

 $R^3$  and  $R^5$  can alternatively be taken together to form -CH2CH2CH2-; or  $R^4$  and  $R^5$  can alternatively be taken together to form -(CH2)u-, where u=2-5;

K is an L-isomer amino acid of structure  $-N(R^6)CH(R^7)C(=0)$ -, wherein:

R<sup>6</sup> is H or C1-C8 alkyl;

 $R^7$  is:

$$-(CH2)q$$

$$-(CH2)q$$

$$NH2;$$

$$NH2;$$

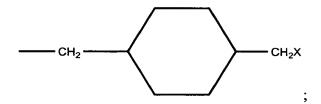
$$NH2, where q = 0 or 1;$$

-(CH2)rX, where r = 3-6;

**Application No.:** 09/534,893

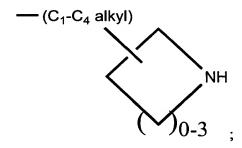
Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116



-(CH2)mS(CH2)2X, where m = 1 or 2;

-(C3-C7 alkyl)-NH-(C1-C6 alkyl);



-(CH2)m-O-(C1-C4 alkyl)-NH-(C1-C6 alkyl), where m = 1 or 2;

-(CH2)m-S-(C1-C4 alkyl)-NH-(C1-C6 alkyl), where m=1 or 2; and

X is -NH2 or -NHC(=NH)(NH2), provided that X is not -NH2 when r = 4; or

R<sup>6</sup> and R<sup>7</sup> are alternatively be taken together to form

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

L is -Y(CH2)vC(=O)-, wherein:

Y is NH, O, or S; and v = 1,2;

$$\begin{array}{c|c}
R^{17} & H & C \\
 &$$

M is a D-isomer or L-isomer amino acid of structure

wherein:

q' is 0-2;

R<sup>17</sup> is H, C1-C3 alkyl;

R<sup>8</sup> is selected from:

-CO2R<sup>13</sup>,-SO3R<sup>13</sup>, -SO2NHR<sup>14</sup>, -B(R<sup>34</sup>)(R<sup>35</sup>), -NHSO2CF3, -CONHNHSO2CF3, -PO(OR<sup>13</sup>)2, -PO(OR<sup>13</sup>)R<sup>13</sup>, -SO2NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O), -SO2NH-heteroaryl (said heteroaryl being 5-10-membered and having 1-4 heteroatoms selected independently from N, S, or O), -SO2NHCOR<sup>13</sup>, -CONHSO2R<sup>13a</sup>, -CH2CONHSO2R<sup>13a</sup>, -NHSO2 NHCOR<sup>13a</sup>, -NHCONHSO2R<sup>13a</sup>, -SO2NHCONHR<sup>13</sup>.

24. (previously added) The method of Claim 20 wherein the localization step comprises the step of localizing a compound of the formula (IV) at the pulmonary embolus:

## 25. (canceled)

- 26. (previously added) The method of Claim 17 wherein the acquisition step comprises the step of acquiring image slices representing a concentration of radioactivity associated with the pulmonary embolus.
- 27. (previously added) The method of Claim 26 wherein the acquisition step comprises the step of acquiring single photon emission computed tomography images of the pulmonary embolus.
- 28. (previously added) The method of Claim 17 wherein the acquisition step comprises the step of acquiring transaxial image slices and further comprising the step of reformatting the transaxial image slices into image slices that are parallel to a long axis associated with the pulmonary embolus.

**Application No.:** 09/534,893

Office Action Dated: April 11, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

29. (previously added) The method of Claim 17 comprising the step of displaying the two-dimensional array as a reprojected image.

- 30. (previously added) The method of Claim 17 wherein the scanning step is performed at a series of angles.
- 31. (previously added) The method of Claim 30 wherein the assignment step is performed at each of the series of angles.
- 32. (previously added) The method of Claim 31 comprising the step of sequentially displaying the two-dimensional arrays as reprojected images.
  - 33-54. (canceled)
- 55. (previously added) The method of Claim 20 comprising the step of displaying the two-dimensional array as a reprojected image.
- 56. (previously added) The method of Claim 20 wherein the scanning step is performed at a series of angles.
- 57. (previously added) The method of Claim 56 wherein the assignment step is performed at each of the series of angles.
- 58. (previously added) The method of Claim 57 comprising the step of sequentially displaying the two-dimensional arrays as reprojected images.